ASTHMA AND ALLERGIC DISEASES

Allergies are the result of inappropriate immune responses to normally harmless substances. Allergy symptoms vary widely, from the sneezes, watery eyes, and congested nose of mild "hay fever" to severe rashes, swelling, and shock. Asthma is a chronic inflammation of the lungs that airborne allergens can trigger in susceptible people; tobacco smoke, air pollution, viral respiratory infections, or strenuous exercise can also contribute. Asthma and allergic diseases can significantly decrease quality of life, employee productivity, and school attendance; in severe cases, they can be life threatening. The goal of NIAID's asthma and allergic diseases research program is to develop more effective treatments and prevention strategies.

Allergies are the sixth leading cause of chronic disease in the United States and cost the healthcare system $18 billion annually.[15] About half of all Americans test positive for at least one of the 10 most common allergens[16] (ragweed, Bermuda grass, rye grass, white oak, Russian thistle, *Alternaria* mold, cat, house dust mite, German cockroach, and peanut), and about 50 million suffer from allergic diseases each year. Food allergy occurs in 6 to 8 percent of children aged 6 years or younger and in 2 percent of adults.[17] Common food allergens include cow's milk, eggs, shellfish, and nuts; peanuts and tree nuts are the leading causes of fatal and near-fatal food allergy reactions.

The prevalence of asthma is also high. In 2002, 20 million people living in the United States currently had asthma; approximately 12 million people, including 4.2 million children younger than 18 years, had experienced an asthma attack in the previous 12 months.[18] Asthma is much more prevalent among non-Hispanic Blacks than among non-Hispanic Whites and Hispanics, especially in children. For reasons that are still unclear, the prevalence of both allergy and asthma in the United States is increasing.

Magnified image of the common dust mite, which causes allergic responses in people.

The causes, pathogenesis, diagnosis, treatment, and prevention of asthma and allergic diseases are major areas of emphasis for NIAID's Division of Allergy, Immunology, and Transplantation. NIAID vigorously pursues research on asthma and allergic diseases by supporting investigator-initiated projects, cooperative clinical studies, a national network of research centers, and demonstration and education research projects.

In 2004, NIAID invited applications to establish the Food Allergy Research Consortium, a collaborative research program designed to develop new approaches to treat and prevent food allergy. The program goals are to develop immune intervention strategies for preventing and treating food allergy; identify the mechanisms of development, loss and re-emergence of oral tolerance; determine the molecular and functional characteristics of food allergens; and determine the role of the gastrointestinal tract in development and loss of oral tolerance.

The Inner-City Asthma Study, co-funded by NIAID and the National Institute of Environmental and Health Sciences (NIEHS), was a multicenter, randomized controlled trial that tested the effectiveness of two interventions in reducing asthma morbidity among inner-city children with moderate to severe asthma; the study concluded in 2001. One intervention provided physicians with more detailed and up-to-date information on participants' recent asthma symptoms and medication use. The other

intervention reduced exposure to environmental triggers such as tobacco smoke and allergens derived from cockroaches, house dust mite, mold, furry pets, and rodents. Participants were evaluated during both the 1-year intervention and for a 1-year follow-up period. The environmental intervention substantially lowered levels of cockroach and house dust mite allergens in the patients' environments, and this reduction was directly related to a decrease in asthma symptoms. The results of this study highlight the role of indoor allergens and tobacco smoke in determining asthma severity in inner cities and demonstrate that environmental interventions can substantially improve symptoms.

One project within the Inner-City Asthma Study evaluated the impact of indoor and outdoor fine particles and co-pollutants on respiratory illnesses. Recently published data from this study, which was funded by NIAID, NIEHS, and the U.S. Environmental Protection Agency, demonstrate that approximately 25 percent of the indoor particle concentration is contributed by outdoor particles. These data also show that smoking is the major source of indoor particles and that indoor concentrations of fine particles peak in the late evening in homes where smoking occurs, perhaps reflecting the influence of after-dinner smoking. Analysis of data pertaining to the effects of particle concentrations on asthma symptoms is currently underway.

The Inner-City Asthma Consortium (ICAC) is a NIAID-funded research network that evaluates the safety and efficacy of immune-based therapies to reduce asthma severity and prevent disease onset in inner-city children, investigates the mechanisms of action of the immune-based therapies, develops and validates biomarkers of disease progression, and investigates the immunopathogenesis of asthma in inner-city children. In FY 2004, ICAC initiated a cockroach allergen standardization protocol, a study to evaluate the usefulness of measurements of exhaled nitric oxide in the clinical management of asthma in children, and a birth cohort to investigate the allergic and environmental factors that contribute to the development of asthma in inner-city children. The birth cohort project is being conducted at four sites and will enroll 500 newborns.

NIAID supports 13 Asthma and Allergic Diseases Research Centers (AADRCs), which are the cornerstone of the pathobiology component of the NIAID asthma and allergy research portfolio. The AADRCs conduct basic and clinical research on the mechanisms, diagnosis, treatment, and prevention of asthma and allergic diseases.

NIAID and the National Heart, Lung, and Blood Institute cosponsor the Immune System Development and the Genesis of Asthma program, which supports research on changes in immune function that occur early in life and lead to the development of asthma. Identification of the cellular and molecular processes involved in the onset of asthma will provide the basis for devising novel and effective new immune-based strategies for asthma treatment and prevention that do not compromise the integrity of the immune system.

The Immune Tolerance Network (ITN) is an international consortium of basic scientists and clinical investigators that performs clinical research to evaluate the safety and efficacy of methods that can induce the immune system to tolerate certain antigens, including allergens, for the treatment of immune-mediated disorders. ITN, which is co-sponsored by NIAID, the National Institute of Diabetes and Digestive and Kidney Diseases, and the Juvenile Diabetes Research Foundation International, has completed one trial of DNA-ragweed allergen conjugates for the treatment of allergic rhinitis. Preliminary data suggest that patients who received this conjugate prior to the 2001 ragweed season experienced fewer allergy symptoms during both the 2001 and 2002 ragweed seasons. ITN is currently conducting a phase II placebo-controlled trial to evaluate the safety and efficacy

of another treatment for ragweed allergy, which involves treatment with omalizumab, an anti-IgE antibody, and immunotherapy. A followup study will examine whether this treatment creates persistent immunologic and clinical tolerance. More information on ITN is available at *www.immunetolerance.org*.

In FY 2004, NIAID established the Atopic Dermatitis and Vaccinia Network to develop short- and long-term approaches to reduce the incidence and severity of eczema vaccinatum and protect individuals with atopic dermatitis from adverse consequences of vaccinia exposure.

An important NIAID intramural study is examining how allergen immunotherapy (AIT) reduces or prevents reactions to allergens such as pollen, dust, or cat dander. Although the efficacy of AIT in asthma is modest, it is nonetheless the only disease-modifying therapy for allergic asthma currently known. Certain types of white blood cells, called Th2 cells, produce substances that contribute to the development of allergies, while others, called Th1 cells, produce substances that may inhibit the development of allergies. This study will determine whether AIT changes the immune response to allergens by reducing the number of Th2 cells or by converting them into Th1 cells. A better understanding of the mechanisms underlying the clinical effectiveness of AIT might help scientists to discover new approaches to treating allergies and asthma.